Real-world Health Care Expenditures Associated With Standard & Extended Half-Life Recombinant Factor IX Products for Management of Severe Hemophilia B

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INTRODUCTION

- Hemophilia B, caused by a deficiency of coagulation factor IX (FIX), represents 15% to 20% of all hemophilia cases and occurs in 1 in 30,000 live male births across all racial/ethnic groups[1,2]
- Replacement of FIX coagulation factor is the standard of care for the treatment and prevention of bleeding events and their potential complications[1]
- Plasma-derived and recombinant FIX (rFIX) products have half-lives of ≈18–24 hours[1,3]
  - With pharmacokinetic sampling up to 96 hours, the terminal half-life of the first rFIX, nonacog alfa (BeneFIX; Pfizer Inc, Philadelphia, PA, USA), is ≈40 hours[4]
- Through fusion of FIX with the Fc region of immunoglobulin G, eftrenonacog alfa (Alprolix; Biogen, Cambridge, MA, USA) was developed, with a half-life of ≈82 hours[3]
  - The price per international unit (IU) of this extended half-life (EHL) product exceeds that of standard half-life (SHL) products, and cost analysis scenarios for transitioning patients have been reviewed[5]
- A newer EHL factor product created by fusion of rFIX to human recombinant albumin, albutrepenonacog alfa (Idelvion; CSL Behring, King of Prussia, PA, USA), has a half-life of ≈92 hours[3,6]
- Limited data are available regarding real-world dispensation and expenditures associated with the use of SHL versus EHL FIX replacement products in the management of hemophilia B

OBJECTIVE

- An analysis of real-world claims data for US patients with severe hemophilia B who were receiving a prophylactic treatment regimen was conducted to assess the expenditures and factor IUs dispensed associated with nonacog alfa, an SHL product, compared with the EHL products eftrenonacog alfa and albutrepenonacog alfa

METHODS

- Data from a large US national specialty pharmacy dispensation claims database for male patients with a diagnosis code of ICD-9 286.1/ICD-10 D67 who had used nonacog alfa, eftrenonacog alfa, or albutrepenonacog alfa from May 2016 to December 2017 were evaluated
- Availability of clinical characteristics allowed for restriction of the analyses to patients with severe hemophilia B and those on prophylactic regimens only
- Key outcome measures were monthly direct expenditures and number of metric factor IUs dispensed
  - Expenditures were calculated using the metric IUs dispensed and the per-unit wholesale acquisition cost (WAC) prices for nonacog alfa, eftrenonacog alfa, and albutrepenonacog alfa for each specific month (**Table 1**)

Table 1. Per-Unit WAC Prices for 2016 and 2017 for Nonacog Alfa, Eftrenonacog Alfa, and Albutrepenonacog Alfa

Drug	2016 per-unit WAC	2017 per-unit WAC
Nonacog alfa	$1.37	$1.37
Eftrenonacog alfa	$2.85 (prior to July 1) $2.97 (beginning July 1)	$3.03
Albutrepenonacog alfa	$4.25	$4.25

WAC, wholesale acquisition cost.

- Monthly means were calculated for each patient by summing all available monthly values for individual patients, then dividing by the number of months from the first to the last month in which data were available, inclusive of months when no product was dispensed
- Data were summarized descriptively (means, standard deviation [SD], medians, minimums, and maximums)
- The Wilcoxon 2-sample test was used to compare expenditures and IUs dispensed between the SHL and EHL products)

RESULTS

- A total of 162 patients met the entry criteria; nonacog alfa was dispensed to 87 patients, eftrenonacog alfa was dispensed to 67 patients, and albutrepenonacog alfa was dispensed to 33 patients
  - The nonacog alfa and eftrenonacog alfa treatment groups included 25 patients who had received both products during the study period
- The eftrenonacog alfa treatment group had a smaller proportion of patients aged <18 years and larger proportions of patients aged 18–39 and 40–59 years than the nonacog alfa and albutrepenonacog alfa treatment groups, which shared similar age distributions (**Table 2**)

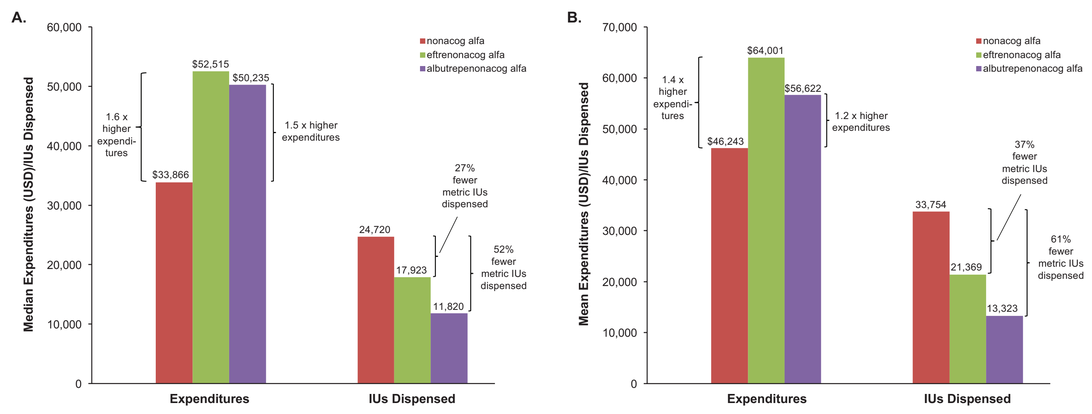
Table 2. Patient Demographics

Characteristic	Nonacog alfa (n=87[a])	Eftrenonacog alfa (n=67[a])	Albutrepenonacog alfa (n=33)
Age group, years, n (%)			
<18	53 (60.9)	26 (38.8)	21 (63.6)
18–39	24 (27.6)	24 (35.8)	8 (24.2)
40–59	8 (9.2)	15 (22.4)	4 (12.1)
≥60	2 (2.3)	2 (3.0)	0
Diagnosis code, n (%)			
ICD-9 286.1	3 (3.5)	1 (1.5)	0
ICD-10 D67	84 (96.6)	66 (98.5)	33 (100.0)

[a]25 patients received nonacog alfa and eftrenonacog alfa during the study period and are included in both columns.
Combined percentages may not equal 100% due to rounding.

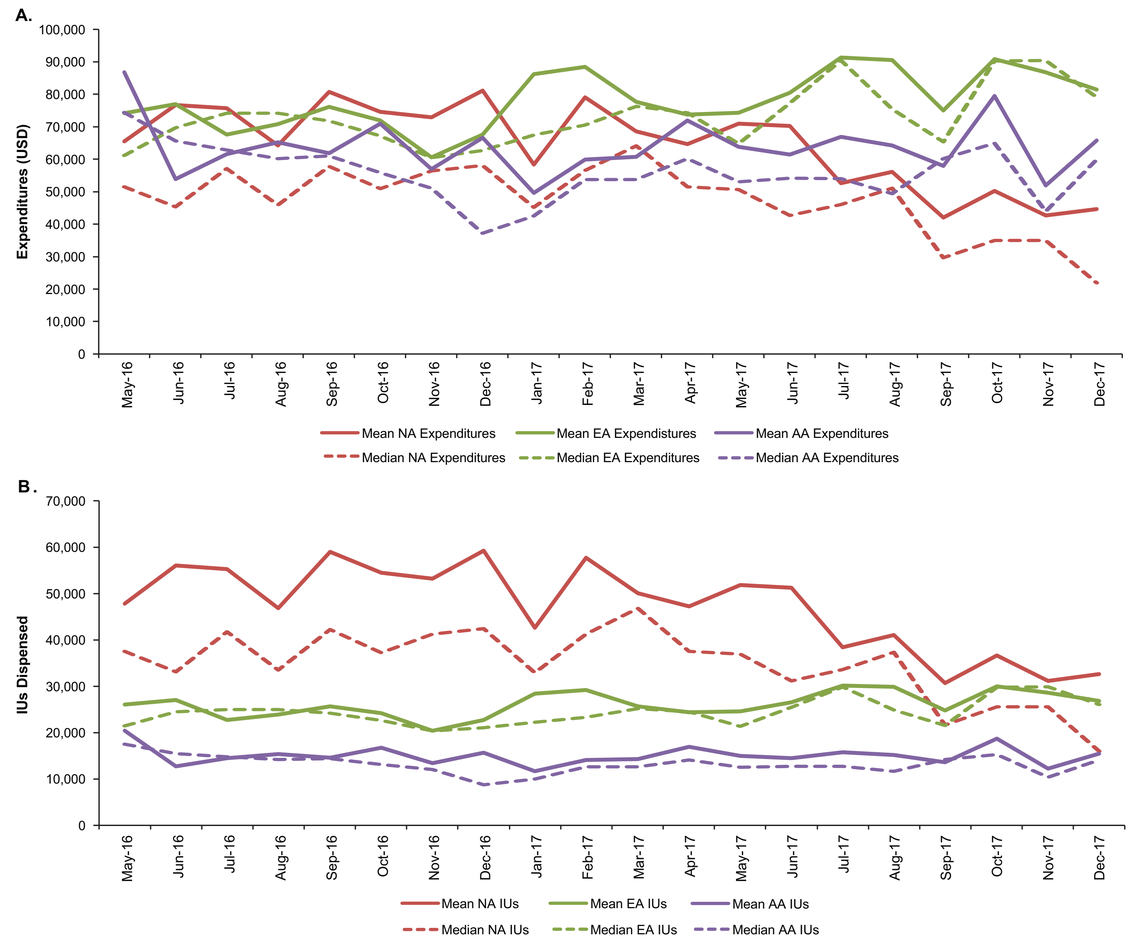
- Median monthly average expenditures in the eftrenonacog alfa treatment group and the albutrepenonacog alfa treatment group were 1.6 times higher and 1.5 times higher, respectively, than in the nonacog alfa treatment group; these differences were statistically significant (eftrenonacog alfa vs. nonacog alfa, *P*=.0004; albutrepenonacog alfa vs. nonacog alfa, *P*=.0267; **Figure 1A**)
  - The range of median monthly average expenditures was $21,920 to $64,116 for the nonacog alfa treatment group, $60,463 to $90,447 for the eftrenonacog alfa treatment group, and $37,196 to $74,392 for the albutrepenonacog alfa treatment group (**Figure 2A**)
- Mean monthly average expenditures in the eftrenonacog alfa treatment group and the albutrepenonacog alfa treatment group were 1.4 times higher and 1.2 times higher, respectively, than in the nonacog alfa treatment group (**Figure 1B**)
  - The range of mean monthly average expenditures was $42,028 to $81,148 for the nonacog alfa treatment group, $60,578 to $91,322 for the eftrenonacog alfa treatment group, and $49,625 to $86,791 for the albutrepenonacog alfa treatment group (**Figure 2B**)
- The median monthly average of IUs dispensed in the eftrenonacog alfa treatment group and the albutrepenonacog alfa treatment group were 27% lower and 52% lower, respectively, than in the nonacog alfa treatment group; these differences were statistically significant (eftrenonacog alfa vs. nonacog alfa, *P*=.004; albutrepenonacog alfa vs. nonacog alfa, *P*<.0001; **Figure 1A**)
  - The range of median monthly average IUs dispensed was 16,000 to 46,800 for the nonacog alfa treatment group, 20,358 to 29,851 for the eftrenonacog alfa treatment group, and 8,752 to 17,504 for the albutrepenonacog alfa treatment group (**Figure 2B**)
- The mean monthly average of IUs dispensed in the eftrenonacog alfa treatment group and the albutrepenonacog alfa treatment group were 37% lower and 61% lower, respectively, than in the nonacog alfa treatment group (**Figure 1B**)
  - The range of mean monthly average IUs dispensed was 30,677 to 59,232 for the nonacog alfa treatment group, 20,397 to 30,139 for the eftrenonacog alfa treatment group, and 11,677 to 20,421 for the albutrepenonacog alfa treatment group (**Figure 2B**)

Figure 1. Median (A) and Mean (B) Expenditures and International Units Dispensed for Nonacog Alfa, Eftrenonacog Alfa, and Albutrepenonacog Alfa (National Specialty Pharmacy Dispensation Claims Database)



IU, international units; USD, US dollars.

Figure 2. Median and Mean Monthly Expenditures (A) and IUs Dispensed (B) for Nonacog Alfa, Eftrenonacog Alfa, and Albutrepenonacog Alfa From May 2016 to December 2017 (National Specialty Pharmacy Dispensation Claims Database)



AA, albutrepenonacog alfa; EA, eftrenonacog alfa; IU, international units; NA, nonacog alfa; USD, US dollars.

Study Limitations

- This analysis was retrospective in nature and was limited by data availability within the claims database
  - Information about disease severity and treatment regimen was available; however, the database did not include information on the number of bleeding events or about patient adherence to treatment
- While the claims data showed that a prescription was filled, there was no confirmation that the factor was actually administered
- Studies of rare diseases, such as hemophilia, are challenging because of small sample sizes and geographically diverse populations[7]
- Reasons for month-to-month variation in factor IUs dispensed (and subsequent expenditures) could include changes in prescribed prophylactic regimens, presence or absence of bleeding events requiring treatment, need for surgery, trauma to the patient, and use of stockpiled factor units by the patient
- The effects of discounts or distribution prices on the expenditures analysis were not known and could not be considered in this analysis

CONCLUSIONS

- This analysis of a large, national pharmacy dispensation claims database was tailored to include clinical parameters identifying patients with severe hemophilia B who were receiving prophylactic treatment with an SHL and/or EHL FIX replacement product
- In this study using real-world data, despite fewer factor IUs dispensed in the EHL groups compared with the SHL group, the differences did not meet proposed per-patient reductions[5,8] and expenditures remained higher in the EHL groups
  - This finding suggests that cost parity for patients with severe hemophilia B receiving prophylactic treatment was not achieved with the EHL products
- Further analyses to validate these findings across additional patient populations should be explored

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AUTHOR DISCLOSURES

A Chhabra, D Spurden, PF Fogarty, B Tortella, E Rubinstein, S Harris, and J Alvir are employees of Pfizer Inc and own stock/options in the company. A Pleil was an employee of Pfizer Inc at the time of this analysis.

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